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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/917,372	07/27/2001	Preeti G. Lal	PC-0050 US	1477

7590 06/17/2003

LEGAL DEPARTMENT
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EXAMINER	
O HARA, EILEEN B	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 06/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/917,372	LAL ET AL.	
	Examiner	Art Unit	
	Eileen O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *8-22* is/are withdrawn from consideration.

5)☒ Claim(s) *3* is/are allowed.

6)☒ Claim(s) *1,2 and 4-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-22* ~~are~~ was subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 1-22 are pending in the instant application. Claim 1 has been amended as requested by Applicant in Paper Number 6, filed February 27, 2003.

Election/Restriction

2. Applicant's election with traverse of Group I in Paper No. 6 is acknowledged. The traversal is on the ground(s) that claims 8-11 of Group II and claims 12 and 13 of Group III are methods of use of the polynucleotides of Group I that are limited in scope to the composition of matter of these claims and could therefore be examined together with the claims of Group I without undue burden. Applicants note that Group I already contains a method of use of the polynucleotide in making a protein and the Examiner has also included a method of use of the polypeptides of the invention of Group IV together with the compositions of matter of the polypeptides and therefore does not consider the examination of method claims and composition of matter claims together in those instances to be an undue burden.

This is not found persuasive because consistent with current patent practice, a serious search burden may be established by (A) separate classification thereof: (B) a separate status in the art when they are classifiable together: (C) a different field of search:. These criteria were met in the above restriction. Also, what was done with the protein and methods of use are not binding for the nucleic acids and methods of use. According to MPEP 821.04, claims drawn to product and method of using the product are properly restrictable and that claims drawn to the non-elected invention will be withdrawn from consideration. Applicant is free to request

rejoinder under *In re Ochiai*. Once elected claims, that is product claims, are found allowable, withdrawn process claims which include all the limitations of the allowable product claims can be rejoined in accordance with *In re Ochiai*. This last point is important and applicants should be careful to maintain identical scopes for the products of Group I and processes of Groups II and III if rejoinder is desired once the product claims are found allowable. Further, as shown by the Groups' different classification and the fact that a search for the polynucleotide does not require a search for the method, it is maintained that it would require a serious burden to search both Groups I, II and III.

The requirement is still deemed proper and is therefore made FINAL.

Claims 8-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 6.

Claims 1-7 are currently under examination.

Specification

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Nucleic acids encoding TNF receptor 2 related protein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 2 and 4-7 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification describes a nucleic acid sequence (SEQ ID NO: 2) and encoded polypeptide sequence consisting of SEQ ID NO: 1, identified as human TNFR2PV (Tumor Necrosis Factor receptor 2 related protein variant), which is identical to human TNFR2P (Tumor Necrosis Factor receptor 2 related protein, also known as lymphotoxin β receptor, LTβ-R), except that the TNFR2PV of the instant invention lacks the 36 amino acid transmembrane domain present in TNFR2P/LTβ-R (Figure 2, alignments of TNFR2PV with human and mouse LTβ-R). This deleted portion occurs after amino acid 223 of the protein of SEQ ID NO: 1. Therefore, the protein of the instant invention is most likely a soluble form of the human LTβ-R, which is a receptor for the cell-surface LTα-LTβ complex. It is well known in the art that membrane bound receptors can also naturally occur in soluble form and still bind the natural ligand (see Wallach, D. (2000) TNF ligand and TNF/NGF receptor families. In: Cytokine Reference (Joost J. Oppenheim and Marc Feldmann editors in chief). Academic Press (London), pages 377-411, especially page 377, second column, bottom paragraph).

The claims as written include nucleic acids comprising fragments and homologues or nucleic acids encoding polypeptides comprising fragments and homologues, and encompass polypeptides that vary substantially in length and also in amino acid composition. The instant disclosure of a single polypeptide, that of SEQ ID NO: 1 with the instantly disclosed specific activity, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, a single isolated polypeptide sequence SEQ ID NO: 1, and the highly related human and mouse prior art LTβ-R proteins. Protein function, however, cannot be reliably predicted from protein sequence homology. For example, Transforming Growth Factor (TGF-beta) Family OP-1 induces metanephrongenesis whereas closely related TGF-beta family members-BMP-2 and TGF-beta1-have no effect on metanephrogenesis under identical conditions (Vukicevic et al., 1996, PNAS USA 93:9021-9026). Platelet-derived Growth Factor (PDGF) Family VEGF, a member of the PDGF family, is mitogenic for vascular endothelial cells but not for vascular smooth muscle cells while PDGF is mitogenic for vascular smooth muscle cells but not for vascular endothelial cells (Tischer et al., U.S. Patent 5,194,596, column 2, line 46 to column 3, line 2). Finally, vertebrate growth hormone of 198 amino acids becomes an antagonist (inhibitor of growth) when a single amino acid is changed (Kopchick et al, U.S. Patent No. 5,350,836). Even 99% homology does allow predictability in this instance. Given the unpredictability of homology comparisons, and the fact that the specification fails to provide objective evidence that the additional sequences are indeed species of the claimed genus it cannot be established that a representative number of species have been disclosed to support the genus claim. No activity is set forth for the additional sequences. The instantly claimed genus is not so limited and the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify the polynucleotides encompassed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 4 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5.1 Claim 4 is indefinite because it encompasses a composition comprising a cDNA and a labeling moiety, and it is not clear if the labeling moiety is covalently attached to the cDNA or is separate.

5.2 Claim 7 is indefinite because it encompasses a method of using the cDNA of claim 1 to produce a protein, and since the cDNA of claim 1 can be the coding sequence (encodes the protein of SEQ ID NO: 1) or the complement of the coding sequence which would not encode the protein of SEQ ID NO:1, it is not clear what protein would be produced.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1, 2 and 4-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Baens et al., Genomics, Vol. 16, pages 214-218, August 3, 1993.

Claims 1, 2 and 4-6 encompass an isolated cDNA comprising a nucleic acid sequence encoding a protein of SEQ ID NO:1, antigenic fragment of SEQ ID NO:1 from about amino acid

residue P216 to about amino acid residue P235 of SEQ ID NO:1, and a naturally occurring variant of the amino acid sequence of SEQ ID NO: 1 at least 95% identical to SEQ ID NO: 1, an isolated cDNA comprising a nucleic acid sequence of a fragment of SEQ ID NO: 2 selected from SEQ ID NOS: 7-9 and a variant of SEQ ID NO: 2 having at least 85% identity to SEQ ID NO: 2, composition comprising the cDNA of claim 1 and labeling moiety, vector and host cell comprising the cDNA of claim 1.

Baens et al. disclose a cDNA identified as CD18-9 (see page 217, paragraph bridging columns 1 and 2) that is identical to nucleotides 51-1982 of SEQ ID NO: 2 except for three mismatches at nucleotide 1420, 1461 and 1714, and a 108 nucleotide insertion (see attached sequence alignment). This cDNA is 91.3% identical to the nucleotide sequence of SEQ ID NO: 2 of the instant application and is therefore a variant of SEQ ID NO: 2 having at least 85% identity to SEQ ID NO: 2. Since the cDNA of Baens et al. **comprises** a nucleic acid sequence of SEQ ID NOS: 7-9 (ranging from nucleotides 629-1378 of SEQ ID NO: 2, specification at page 8), Baens et al. also meets the limitation of claim 2, part b. Claim 2 does not have a limitation that the nucleic acid sequences are contiguous. The cDNA of Baens et al. encodes a protein that is identical to the amino acid sequence of SEQ ID NO: 1 of the instant invention, except that the protein of SEQ ID NO: 1 is missing a 36 amino acid segment, which corresponds to the transmembrane domain of the protein of Baens et al. (see attached alignment). Since claim 1 recites "An isolated cDNA,……., **comprising** an nucleic acid sequence encoding a protein", and the cDNA of Baens et al. does encode the protein of SEQ ID NO: 1, the cDNA of Baens et al. meets the limitations of the claims. There is no limitation that the nucleic acid encodes contiguous amino acids. Baens et al. also discloses vector and host cell comprising the cDNA

(page 215, first column, fifth full paragraph), and hybridization of the clone to Southern blots (page 217, second column, lines 4-7). Although Baens et al. do not specifically state that the cDNA was labeled or in a composition comprising a labeling moiety, the cDNA would have to have been labeled by necessity to probe a Southern blot. Additionally, Baens et al. do teach labeling of the heterogeneous nuclear complementary (hnc) DNA used to screen a cDNA library to isolate the full-length cDNA clone of CD18-19 (see page 215, first column, first full paragraphs 3-5).

This rejection could be overcome by adding limitations in which the sequences must be contiguous.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Baens et al., Genomics, Vol. 16, pages 214-218, August 3, 1993, in view of Sibson et al. WO 94/01548.

Claim 7 encompasses a method for using a cDNA to recombinantly produce a protein. The teachings of Baens et al. are summarized as above. Baens et al. does not teach recombinant production of protein.

Sibson et al. disclose that it is generally useful to place a desired cDNA sequence into an expression vector and host cell and to express the encoded protein (see pages 8-13).

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to use the cDNA of Baens et al., in an expression vector and host cell, to express and then isolate the encoded polypeptide, as taught by Sibson et al., in view of Sibson et al.'s suggestion that it would be desirable to do so, as cited above. The skilled artisan would be motivated to do so in order to easily produce and analyze the encoded protein to determine its biological activity, and since Baens et al. taught that the cDNA CD18-9 encoded a predicted protein that appeared to be a member of the family of tumor necrosis factor (TNF) receptor-related proteins, one of ordinary skill in the art would be motivated to produce such a protein, since members of the TNF receptor family are known to be involved in a large number of diseases and disorders, and a new member of the family could potentially be medically important. There would be a reasonable expectation of success, since the method of recombinantly producing protein is routinely and successfully used in the field of molecular biology.

Conclusion

8.1 Claim 3 is allowed.

8.2 Claims 1, 2 and 4-7 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Eileen B. O'Hara

Patent Examiner